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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/648,089	08/26/2003	Samuel H. Gellman	09820.286	2777

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EXAMINER	
KOSAR, ANDREW D	

ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
10/29/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/648,089	GELLMAN ET AL.	
	Examiner	Art Unit	
	Andrew D. Kosar	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4,6,8,9 and 11* is/are pending in the application.

4a) Of the above claim(s) *8,9 and 11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4 and 6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 August 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 6, 2007 has been entered.

Response to Arguments/Amendments

Applicant's amendments and arguments filed August 6, 2007 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed is herein withdrawn.

Claims 4, 6, 8, 9 and 11 are pending.

Claims 8, 9 and 11 remains withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claim Rejections - 35 USC §§ 101 and 112

35 U.S.C. 101 reads as follows:
Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Applicant's arguments are generally iterative of arguments presented previously. Generally, Applicant asserts that interrupting protein-protein interactions is fully discussed in the

specification, the Gellman declaration "clearly shows that the present compounds have a well-accepted utility consistent with the utility that is disclosed in the specification as filed" and that Seebach and US 6,958,384 are "objective evidence of the utility." (Remarks, page 16).

Applicant continues to assert that disrupting "specific protein-protein interactions" is a credible, specific and substantial utility. Applicant asserts that US 6,958,384 was presented as 'objective evidence' of the utility, and asserts no request was made to have the examiner "pass judgment on the utility or operability of the invention claimed" (Remarks, page 17), as the utility of '384 "is **identical**" (Remarks, page 18). Applicant asserts that Schmitt "is not probative on the question of utility" as it "**is not** contemporaneous in time with the present application," and further argues Kim does not share the same utility and thus is not relevant to the instant inquiry (Remarks, page 18, emphasis in original).

Again, with regards to US 6,958,384, Applicant is kindly directed to MPEP § 716.07, which states in the first line, "Since every patent is presumed valid (35 U.S.C. 282), and since that presumption includes the presumption of operability (*Metropolitan Eng. Co. v. Coe*, 78 F.2d 199, 25 USPQ 216 (D.C.Cir. 1935), **examiners should not express any opinion on the operability of a patent**." (emphasis added). Thus, the comments herein are directed only to the instant Application.

With regards to the instant application, the examiner respectfully disagrees that the instantly claimed compounds have utility under 35 USC § 101 and enablement under 35 USC § 112. Contrary to Applicant's position, the examiner has weighed the objective evidence and has found there to be no support in the instant disclosure or evidence that the utility asserted is credible, substantial and/or specific as required. Furthermore, a single patent does not establish

that the instantly asserted utility was "well-established" such that "a person of ordinary skill in the art would immediately appreciate why the invention is useful," nor does it establish that it is "specific, substantial and credible."

With regards to Schmitt, Applicant asserts that because it is not contemporaneous, it is "not probative of on the question of utility." (Remarks, page 18). Respectfully, the examiner disagrees. If a utility is not accepted as credible, specific or substantial- or in the case of Schmitt, operable, at a later date, it is probative of utility and operability at the time of the invention. Schmitt, contrary to Applicant's assertion, is a similar utility to the instant Application, and is therefore germane to the discussion. Schmitt synthesized similar compounds but only hypothesized on their possible utility, which is also noted to only be a general- not specific- utility, and thus clearly shows that even post-filing, the alleged well-established utility was not widely accepted and readily apparent to the person of ordinary skill.

With regards, to Kim, Kim attempted to create ligands for a specific compound, and found it to be unsuccessful. Kim is germane to the discussion, as the compounds are of a similar structure and do not bind to the specific protein they were designed to bind. Furthermore, as instantly claimed in claim 11, Kim is relevant, as one claimed utility is "mimicking binding interactions" between two protein molecules or fragments thereof *in vitro*, which clearly Kim endeavored- albeit unsuccessfully- to achieve. Thus, , Kim is evidence that the design of compounds for binding to a specific protein is not well-established and is highly unpredictable. If one could not make compounds which bind to a defined specific target (profilin), one would not accept as credible the assertion that the compounds claimed disrupts, or mimics, any protein-

protein interaction, specifically when the specification lacks any single defined interaction being disrupted, probed or mimicked.

As stated previously, extrapolating the generic concept of foldamers inhibiting a generic protein-protein interaction to an experiment blocking Bcl-x_L/BH3 domain interactions is not found in the instant specification as originally filed and nothing would lead the artisan to selection of such an interaction, and thus the declaration and related arguments are not persuasive, as they are not commensurate in scope with the disclosure as filed.

Applicant is reminded that "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. *See Brenner v. Manson*, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.") Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. (*Genentech Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 42 USPQ2d 1001 (Fed. Cir. 1997)).

Claims 4 and 6 are/remain rejected under 35 U.S.C. § 101, for the reasons of record and those set forth below, because the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility.

Claims 4 and 6 are/remain rejected under 35 U.S.C. § 112, first paragraph (enablement), for the reasons of record. Specifically, since the claimed invention is not supported by either a

specific or substantial asserted utility or a well established utility for the reasons set forth under 35 USC § 101, one skilled in the art clearly would not know how to use the claimed invention.

Because Applicant argues the rejection under 35 USC §§ 101 and 112, 1st paragraph, simultaneously, as the rejection under § 112, 1st paragraph, is predicated entirely upon the rejection under § 101, the examiner will address Applicant's remarks in kind.

KIM (Y.J. Kim et al. Bioorg. Med. Chem. Let. (2000) 10, pages 2417-2419) teaches βPro_{10}-Tyr, (previously relied upon under 35 USC § 102). Kim examined "the possibility that β-peptide can substitute for the natural peptide" (page 2418) as a ligand of profilin and that it "failed to bind profilin, whereas the corresponding α-L-proline decamer bound tightly to this protein" (Abstract). Here, Kim provides the possibility of studying the interactions, but determines *inter alia* that the probe is unsuitable, and thus it is inoperative. Without a probe, one cannot study the binding between two proteins.

With regards to Seebach, the Examiner considered the disclosure of Seebach to be inapplicable, as the compounds of Seebach are γ-dipeptides, while the instantly claimed compounds are, at minimum, tetrapeptides with at least 1 α-amino acid and at least 2 cyclically constrained β-amino acids. The compounds are not coextensive or commensurate in scope, and thus cannot provide a 'well established utility' for the instant compounds based upon structure and amino acid content. Furthermore, Seebach merely provides further evidence that the compounds are not of a well established utility, as even Seebach states that the results, "promise a potential of γ-peptides for the development of peptidase-resistant peptidomimetic drugs." (page 777, last paragraph). Seebach makes no reference or inference that the compounds relate to

tetrapeptides (or larger) with α and cyclically constrained β-amino acids that are instantly claimed.

More recently, SCHMITT (M.A. Schmitt, et al. J. Am. Chem. Soc. (2005) 127, pages 13130-13131) teaches compounds which are of a similar structure to those of the instant application (e.g. compound 1). Schmitt, while not contemporaneous with the instant application, provides that the art still does not provide a 'well established' utility, as Schmitt teaches that, "Foldamers of this type [α/β-peptides] might mimic recognition surfaces on proteins and thereby disrupt specific protein-protein interactions [citing Sadowsky (2005)] or perform multifunctional catalysis of chemical reactions." (page 13131, last paragraph). These are general utilities, not specific as required by the statute.

Disruption of protein-protein interactions is a generic utility, and the questions that arise are, "which specific protein-protein interactions are contemplated and disclosed to be disrupted by Applicant?" and, "to what end are the interactions disrupted (e.g. increasing clot formation, preventing angiogenesis, increasing milk production, etc.)?" The specification is silent to any specific protein-protein interaction that is disrupted or what is the effect of the disruption.

While chemical libraries are commercially available, they are sold as research tools, which are clearly delineated by MPEP § 2107.01(I) as being a utility which is not substantial (*see, e.g. page 7, Office Action mailed 5/4/05*). It is noted that the Exhibits do not discuss the particulars of the instant invention, e.g. examples of the instantly claimed compound, but rather generalizations on peptide libraries. Furthermore, as stated in the previous office action the MPEP states, "An assessment that focuses on whether the invention is useful only in a research setting thus does not address whether the invention is in fact "useful" in a patent sense. Instead,

Office personnel must distinguish between inventions that have a specifically identified substantial utility and inventions whose asserted utility requires further research to identify or reasonably confirm." (Emphasis added; *see page 7, Office Action mailed 5/4/05*).

Furthermore, MPEP § 2107 (II)A(3) (the Examination Guidelines for the Utility Requirement) sets forth the test for determining a 'well established utility', stating, "If at any time during the examination, it becomes readily apparent that the claimed invention has a well-established utility, do not impose a rejection based on lack of utility. An invention has a well-established utility if (i) a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention (e.g., properties or applications of a product or process), and (ii) the utility is specific, substantial, and credible." (emphasis added). A 'well-established' utility requires that the utility is specific, substantial and credible, and not a 'general' utility, as is the case in the instant application because there is no specifically identified substantial utility and the invention requires further research and testing to determine what specific protein-protein interactions may be disrupted with the compounds of the instant invention.

Claims 4 and 6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

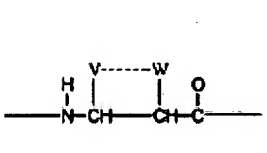
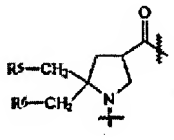
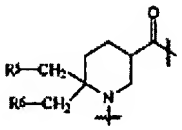
The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter

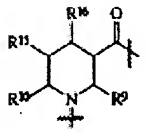
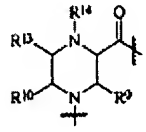
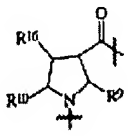
later claimed by him. The courts have stated that, "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated that, "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163. The MPEP does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163. While all of the factors have been considered, a sufficient amount for a *prima facie* case are discussed below.

In the instant case, the claims are drawn generally to isolated unnatural polypeptides of the formula: A-[X_a-Y-Z_c]$_d$-A', X and Z are each an α, β or γ- amino acid, and at least one X or Z is an α-amino acid and at least two of X or Z are two cyclically constrained β-amino acids selected from  ,  and 

  and 

(1) Partial structure:

The claims and specification provide general structural requirement and the specification provides exemplary compounds, however the specification lacks a representative number of examples which are sufficient to adequately provide description for the plurality of compounds embraced by the claims, as the compounds described are structurally similar to each other and do not provide a sufficient variety to describe the genus as a whole.

(3) Physical and/or chemical properties and (4) Functional characteristics:

The claims require no specific function.

(5) Method of making the claimed invention:

Methods of making compounds in general are known to the artisan, however making the myriad of compounds embraced by the claims is beyond that of the artisan.

As stated supra, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that claim(s) 4 and 6 is/are broad and generic, with respect to all possible compounds encompassed by the claims.

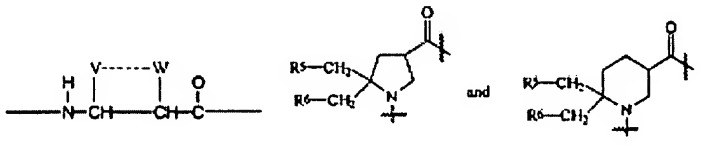
The possible structural variations are limitless to any unnatural polypeptide of the formula: A-$[X_a$-Y-$Z_c]_d$-A', as described generally above. Here, the specification lack sufficient variety of species to reflect the variance in the genus. While having written description of the compounds identified in the specification tables and/or examples, the specification does not provide sufficient descriptive support for the myriad of compounds embraced by the claims.

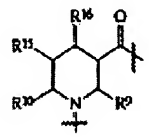
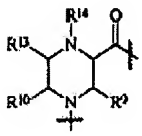
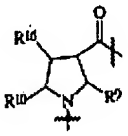
The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Claim Rejections – 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4 and 6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 4 and 6 each recite the Markush group for the cyclically constrained amino acids, such that the residue is selected from  and



and

, and it is unclear and indefinite, as one does not know where the Markush group ends because there are two recitations of 'and' present (between 2nd and 3rd species and between 5th and 6th species).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrew D. Kosar whose telephone number is (571)272-0913. The examiner can normally be reached on Monday - Friday 08:00 - 16:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia J. Tsang can be reached on (571)272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Andrew D Kosar
Patent Examiner
Art Unit 1654